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# 21<sup>st</sup> Century Research in Child Neurology

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The field of Child Neurology encompasses many types of diseases and pathological conditions. These disorders affect a large number of children, and represent a tremendous human, emotional, social and economic burden for our families and society (Boyle et al., 2011). The progressive decrypting of the pathophysiology of psychiatric disorders has led to the blurring of the frontiers between child neurology, pediatric psychiatry, developmental neurobiology, cognitive neurosciences, and social sciences.

Over the last decades, identification of genetic defects responsible for several of these disorders has led to significant advances in our understanding of their pathophysiology (Delorme et al., 2013; Kaindl et al., 2010). In addition, for several diseases, environmental factors seem also to play a key role. The interplay between these environmental factors and genetic factors, probably through epigenetic mechanisms, is probably crucial during brain development, leading to altered programs of neuronal differentiation and connectivity (Hagberg et al., 2015; Boivin et al., 2015). A growing concept is that glial cells (astrocytes, oligodendrocytes, and microglia) play an important role in many if not all these disorders (van Tilborg et al., 2016; Guizzetti et al., 2014). Another important concept is the window of selective vulnerability of various cell types during ontogenic events that leads to particular patterns of injury in preterm and term newborns (Ferriero and Miller, 2010).

Major contributors in the field of child neurology, pediatric psychiatry, and developmental neurosciences have provided state-of-the-art reviews on some of the hottest topics in this rapidly moving field. Although this Special Issue is not exhaustive in this regard, it will cover several aspects and provide the reader a large overview of the recent and very exciting progress this field has made. It will also highlight some existing controversies that represent a unique opportunity to achieve significant advances in the field.

The first paper “Cellular and molecular introduction to brain development” (Jiang and Nardelli, 2016) sets the stage for this Special issue by reviewing the key cellular, molecular,

and genetic bases of brain development. Figures in this paper nicely illustrate the relationship between development and the disorders that can arise during the ontogeny of particular cell types and mechanisms.

The second paper “Neuronal migration disorders” (Stouffer et al., 2016) gives an overview of neuronal migration disorders with a focus on the role of cytoskeleton in abnormal migration, and on epilepsy as a major consequence of aberrant neuronal positioning.

The third paper “Hypomyelinating disorders: an MRI approach” (Barkovich, 2016) illustrates how MRI has led to the understanding of a unique group of leukodystrophies. Newer techniques in MRI imaging methods allow for quantification of myelination as a potential means of assessing disease course and the effects of proposed treatments.

The fourth paper “Genetic and biochemical intricacy shapes mitochondrial cytopathies” (Turnbull and Rustin, 2016) revisits the concept of mitochondrial disease, covering the complexity of mitochondrial genetics and the multiplicity of the roles ensured by mitochondria in various aspects of cell life and death.

The fifth paper “Unexpected cellular players in Rett Syndrome pathology” (Cronk et al., 2016) continues along the theme of the important role of cell types during brain development by exploring the concept that neurons initiate and non-neuronal cells exacerbate the disease. Understanding this feedback loop will aid in the identification of novel therapies.

The sixth paper “Current understanding and neurobiology of epileptic encephalopathies” (Auvin et al., 2016) clarifies the nomenclature for these specific syndromes and highlights the importance of genetics and neuroinflammatory processes in understanding mechanisms and treatment.

The seventh paper “Controversies in Preterm Brain Injury” (Penn et al., 2016)

highlights critical unresolved questions in the etiology and mechanisms causing preterm brain injury. Involvement of neurons, glia, endogenous factors and exogenous exposures is considered, with a special emphasis on the concept of maldevelopment rather than clastic lesions.

The eighth paper “ Perinatal brain damage: the term infant” (Hagberg et al., 2016) focuses on those conditions arising from disturbances of blood flow and lack of oxygen in the newborn term infant. The review highlights advances made from understanding the pathophysiology of these disturbances, especially hypothermia, but the continued need for adjunctive therapy as understanding improves.

Taken together, these outstanding reviews highlight the exciting advances in our understanding of complex brain disorders of childhood and will provide the reader with provocative ideas for further research and discussion. The better understanding of child neurology disorders will lead, in the future, to better and earlier diagnosis, and especially to the discovery and implementation of new treatments and prevention strategies.

## References

- Boyle, C.A., Boulet, S., Schieve, L.A., Cohen, R.A., Blumberg, S.J., Yeargin-Allsopp, M., Visser, S., Kogan, M.D., 2011. Trends in the prevalence of developmental disabilities in US children, 1997-2008. *Pediatrics*, 127, 1034-1042.
- Delorme, R., Ey, E., Toro, R., Leboyer, M., Gillberg, C., Bourgeron, T., 2013. Progress toward treatments for synaptic defects. *Nature Medicine*, 19, 685-694.
- Kaindl, A.M., Passemard, S., Kumar, P., Kraemer, N., Issa, L., Zwirner, A., Gerard, B., Verloes, A., Mani, S., Gressens, P., 2010. Many roads lead to primary autosomal recessive microcephaly. *Progress in Neurobiology* 90, 363-383.
- Hagberg, H., Mallard, C., Ferriero, D.M., Vannucci, S.J., Levison, S.W., Vexler, Z.S., Gressens, P. 2015. The role of inflammation in perinatal brain injury. *Nature Reviews Neurology*, 11 , 192-208.
- Boivin, M.J., Kakooza, A.M., Warf, B.C., Davidson, L.L., Grigorenko, E.L., 2015. Reducing neurodevelopmental disorders and disability through research and interventions. *Nature*, 527, S155-160.
- van Tilborg, E., Heijnen, C.J., Benders, M.J., van Bel, F., Fleiss, B., Gressens, P., Nijboer, C.H., 2016. *Progress in Neurobiology*, in press.
- Guizzetti, M., Zhang, X., Goeke, C., Gavin, D.P., 2014. Glia and neurodevelopment : focus on fetal alcohol syndrome disorders. *Frontiers in Pediatrics*, 2, 123.
- Ferriero, D.M., Miller, S.P., 2010. Imaging selective vulnerability in the developing nervous system. *Journal of Anatomy*, 17, 429-435.

Jiang, X., Nardelli, J., 2016. Cellular and molecular introduction to brain development. Neurobiology of Disease, this issue.

Stouffer, M.A., Golden, J.A., Francis, F., 2016. Neuronal migration disorders. Neurobiology of Disease, this issue.

Barkovich AJ, 2016. Hypomyelinating disorders: an MRI approach. Neurobiology of Disease  
this issue

Turnbull, D.M., Rustin, P., 2016. Genetic and biochemical intricacy shapes mitochondrial cytopathies. Neurobiology of Disease, this issue.

Cronk JC Derecki NC, Litvak V, Kipnis J. Unexpected cellular players in Rett syndrome pathology. Neurobiology of Disease, this issue.

Auvin S, Cilio MR, Vezzani A. Current understanding and neurobiology of epileptic encephalopathies. Neurobiology of Disease, this issue.

Penn, A.A., Gressens, P., Fleiss, B., Back, S.A., Gallo, V., 2016. Controversies in preterm brain injury. Neurobiology of Disease, this issue.

Hagberg H, Edwards AD, Groenendaal F. Perinatal brain damage: the term infant. Neurobiology of Disease this issue.